PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
K1603-PCT		

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/EP00/08410	29/08/2000	30/08/1999

International Patent Classification (IPC) or national classification and IPC
C12Q1/42

Applicant
K.U. LEUVEN RESEARCH & DEVELOPMENT et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 10 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28/02/2001	14.12.2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/08410

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-48 as originally filed

Claims, No.:

1-32 as received on 29/10/2001 with letter of 29/10/2001

Drawings, sheets:

1/44-44/44 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 33-40

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 8-14, 16,17,23,24, 27-32 (entirely); 18-22, 25 (in part), .

because:

☒ the said international application, or the said claims Nos. 27-32 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 8,17,19-23-24 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☒ the claims, or said claims Nos. 8-14,16-17,19-24 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 8-14, 16,17,23,24, 27-32 (entirely); 18-22, 25 (in part), .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:
see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-7, 26(entirely); 18, 25 (in part).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7, 15,18-22, 25,26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	15,18-22,25
	No:	Claims	1-7,26
Industrial applicability (IA)	Yes:	Claims	1-7,15,18-22, 25,26
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 8-14 relate to the use of compounds selected via the method of claim 1 as anti-parasitic agents. These claims are not clear in the sense of Article 6 PCT because they do not define the subject-matter for which protection is sought (i.e. the use) in terms of the definition of the group of parasites. Moreover these claims are not supported in the sense of Article 6 and Rule 6.3(a) PCT in that the description does not technically support the allegation that these compounds are indeed broadly efficacious as anti-parasitic agents. The only support present is for the notion that some compounds indeed have anti-fungal activity. Claims 8, 17 and 19-22 furthermore fail to define the subject-matter for which protection is sought in terms of the technical features of the compounds which are essential features of the claims.

2. The description is also flawed with respect to the requirement of sufficiency of disclosure (Article 5 PCT) for the subject-matter of claims 8, 17 and 19-23 as it does not disclose any other compounds than the ones of claims 9-14, 18, 24 and 32. As the description fails to derive a teaching relating structural features of the compounds found to the trehalose-6-phosphate phosphatase inhibiting activity there is no ground for extending any claims relating to functionally defined compounds.

3. As for the above reasons the indicated subject-matter have not been the subject of the international search, the IPEA gives no opinion on their aspects of novelty and inventive step.

Re Item IV

Lack of unity of invention

4. The broadest possible problem underlying invention 1 (Claims 1-7) and invention 2 (Claims 14, 18 and 25 in part) is the wish to provide anti-parasitical compounds having intracellular activity (See page 3, lines 24-25). The solution provided thereto is to identify inhibitors of trehalose-6-phosphate phosphatases as defined

in claim 1.

The single general concept resides hence in the teaching that trehalose-6-phosphate phosphatase inhibitors are candidate anti-parasitical compounds. This teaching however can not contribute to inventive step of the compound claimed per se.

A reason is that unity between all claimed inventions requires a partial identity between the technical features provided by the structures of the claimed compounds and their effects, which should be objectively definable on the basis of the originally filed application.
This is directly reflected in the Administrative Instructions under the PCT which are binding to the IPEA:

Without requiring a reference to a prior art document the Administrative Instructions, Annex B, part 1, §(f) instructs the ISA and IPEA for cases like the present one.

Present claim 18 is a single claim defining alternatives, i.e. there is a situation involving "Markush practise" (§(f)).

The Markush grouping shall be regarded as unitary if the alternatives are of a "similar nature" (§(f)).

Similarity in the sense of §(f) is acknowledged if all alternatives fulfil two requirements

1- they must have a common property or activity (requirement f(i)(A))

2- there must be a common structure in all alternatives (significant structural element; requirement f(i)(B)(1)).

If there is no common structure this requirement may be replaced by the requirement that all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains (requirement f(i)(B)(2)). The description does not even refer to a "small portion" of the structure in the sense of §(f)(ii).

The IPEA agrees with the applicant that requirement f(i)(A) is fulfilled, but cannot

discover a structural element linking all alternatives. Moreover, after extensive expert consultation, the IPEA must conclude that there exist no class of chemical compounds in the art of inhibiting trehalose-6-phosphate phosphatases, to which all alternatives belong.

Neither of requirements f(i)(B)(1) or f(i)(B)(2) are fulfilled. In logical consequence there is a lack of unity between any of the alternatives of claim 18 and hence between the alternatives in any claim in which any alternative is a special technical feature.

Accepting that the method of claim 1 would lead to identification of anti-parasitical compounds does, however, not mean that a partial identity between structural features and the effects obtained thereby is established as a basis for a concept which is fit for generalisation and which could technically link the method and the compounds of claims 9-14.

The IPEA stresses that it also considered §(e) which expressly allows certain combinations of different categories of claims. It is noted however that the assumed technical link between any process and products lies in the partial structural identity between all products which is pre-ordained by the manufacture of the products. This link is absolutely absent in the present case in which the alternative compounds originate from separate manufacturing processes (nature of the DIVERSet library) (W6/90).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5. Invention 1:

According to the description the subject-matter of claims 1-7 solves the problem of how to identify compounds that are candidate anti-fungal compounds. The state of the art never disclosed trehalose-6-phosphate phosphatase as a target for anti-fungal drug discovery. This idea is as such novel and non-obvious. However, the present wording of claim 1 relates to obvious subject-matter. Based on basic technical knowledge the skilled man not only could design an inhibitor assay

without investing any inventive merit, but also would do so because there is, not only a reasonable expectation of success but even a certainty that once an assay for an enzyme activity is available inhibitors will be found by adding candidate inhibitors to an activity assay. Neither the description nor the state of the art suggests that this would fail for trehalose-6-phosphate phosphatase.

A method claim meeting the requirements of Articles 5, 6 and 33(2)(3) PCT that is one relating to all essential features materializing the above non-obvious method, i.e. a claim like: "A test method for assessing anti-fungal activity of candidate substances comprising the steps of: (a) - (d)", is not present.

The subject-matter of claim 26 is not inventive in view of C. DE VERGILIO ET AL.: 'Disruption of TPS2, the gene encoding the 100-kDa subunit of the threhalose-6-phosphate synthase/phosphatase complex in Saccharomyces cerevisiae, causes accumulation of threhalose-6-phosphate and loss of trehalose-6-phosphate phosphatase activity.', EUR. J. BIOCHEM., , March 1993, vol. 212, no. , pages 315 to 323. See title.

6. Invention 2:

Invention 2 appears to meet the requirements of Article 33(2)(3) PCT. Claims 14, 18-22 and 25 relate to the use of a specified compound (i.e. the **compound** identified in claim 14), the compound per se and methods involving this compound. Assuming the required limitation to anti-fungal activity it is observed that the state of the art disclosed neither the compound per se nor its use as anti-fungal compound. The **compound** per se identified in claim 14 (Claim 18 in part) and the use of claim 15 (when limited to the **compound** identified in claim 14) and the method of claim 25 (in part) are considered to be novel and non-obvious.

Re Item VII

Certain defects in the international application

7. Invention 1:

Article 6 PCT: Claims 5 and 6 lack support. The only technical support present

relates to fungal cells.

8. **Invention 2:**

Claim 14 relates to the use of a specified compound as anti-parasitic agent. The description only supports in the sense of Article 6 PCT and discloses in the sense of Article 5 PCT only the use as anti-fungal agent. No support and sufficient disclosure is present for the broader anti-parasitic use.

CLAIMS

1. A test method for assessing the activity of candidate substances as inhibitors of trehalose-6-phosphate phosphatase, comprising the steps of:

(a) contacting a candidate inhibitor with a biological medium comprising trehalose-6-phosphate and trehalose-6-phosphate phosphatase;

(b) measuring activity in the medium which depends upon the activity of trehalose-6-phosphate phosphatase;

(c) repeating steps (a) and (b) with further candidate inhibitors; and

(d) selecting at least one candidate inhibitor which reduces by at least 25% the activity of trehalose-6-phosphate phosphatase compared with the same medium without the inhibitor under the same conditions.

2. The method of claim 1, wherein the inhibiting effect of the selected candidate inhibitor is greater than that of N-ethylmaleimide and/or dithiodinitrobenzoate

3. The method of claim 1 or claim 2, further comprising the steps of assessing the activity of a second enzyme involved in the synthesis of trehalose-6-phosphate and selecting inhibitors which reduce the activity of trehalose-6-phosphate phosphatase while maintaining a viable activity of the said second enzyme, i.e. at least 25% of the activity of the second enzyme in the same medium under the same conditions but without the inhibitor.

4. A method according to claim 3, wherein the second enzyme is trehalose-6-phosphate synthase.

5. A method according to any of claims 1 to 4, wherein the biological medium includes sub-cellular organelles or sub-cellular non-organelle components, a cell culture or an animal or plant tissue.

6. A method according to claim 5, wherein the sub-cellular organelles or sub-cellular non-organelle components or the cell culture are obtained from cells from a plant, an insect, a nematode or other worm, a fungus, a bacterium or a protozoa or any other

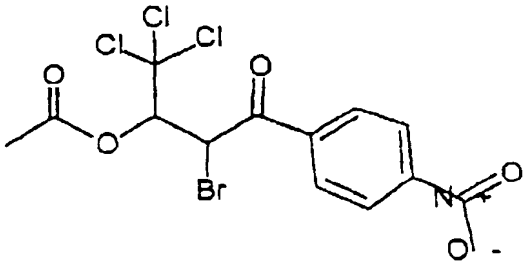
organism expressing trehalose-6-phosphate phosphatase.

7. A method according to any of claims 1 to 6, wherein step (a) is carried out *in vitro* and wherein the method further comprises, after step (d), the steps of:

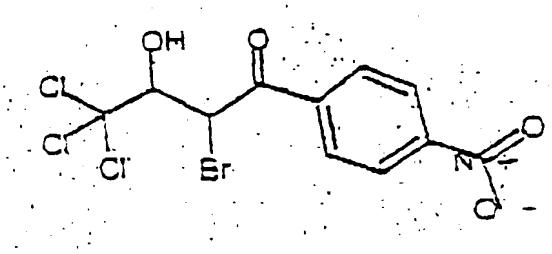
- contacting the candidate inhibitors selected in step (d) with a biological medium comprising whole cells having trehalose-6-phosphate phosphatase as an intracellular enzyme; and
- selecting those candidate inhibitors which reduce the growth of the cells.

8. Use of a trehalose-6 phosphate phosphatase inhibitor selected by a test method according to any of claims 1 to 7 as an antiparasitic agent.

9. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula or a derivative thereof:

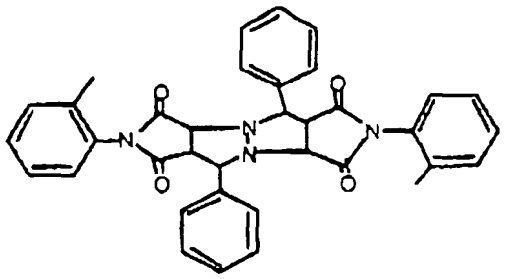


or the structural formula



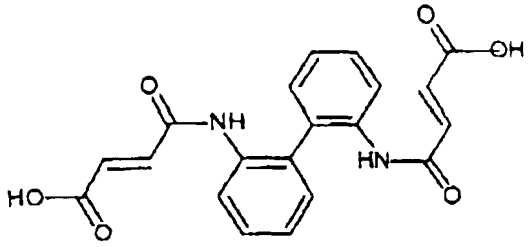
or a pharmaceutically acceptable salt, ester or pro-drug thereof.

10. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula:



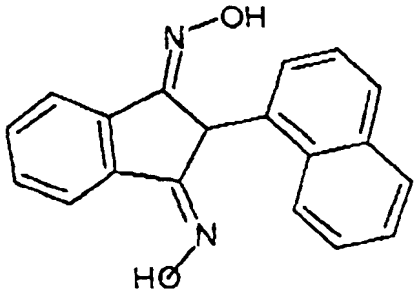
or a pharmaceutically acceptable salt, ester or pro-drug thereof .

11. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula:



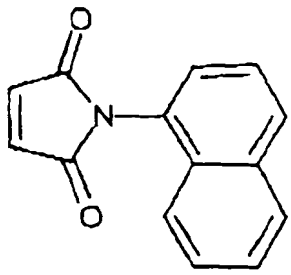
or a pharmaceutically acceptable salt, ester or pro-drug thereof as an antiparasitic agent.

12. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula:



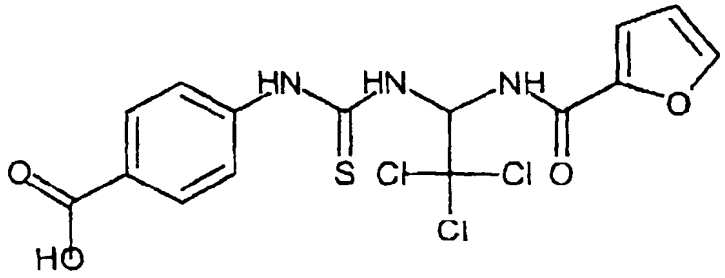
or a pharmaceutically acceptable salt, ester or pro-drug thereof .

13. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula:



or a pharmaceutically acceptable salt, ester or pro-drug thereof .

14. Use according to claim 8, wherein the trehalose-6 phosphate phosphatase inhibitor is a substance with the structural formula:



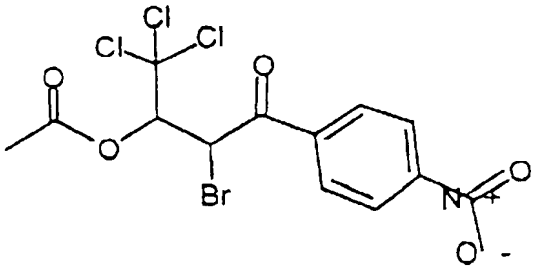
or a pharmaceutically acceptable salt, ester or pro-drug thereof as an antiparasitic agent.

15. Use according to any of claims 8 to 14, wherein the trehalose-6 phosphate phosphatase inhibitor is used as an antifungal agent.

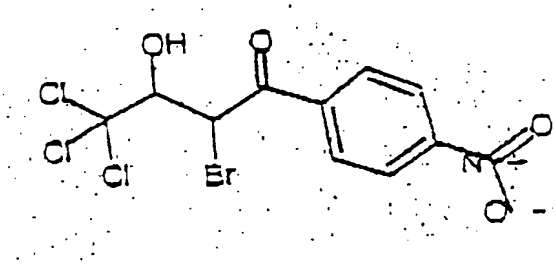
16. Use according to any of claims 8 to 15 , in combination with another antiparasitic agent and/or a compound that induces or enhances the stress response of cells.

17. A biologically, prophylactically or therapeutically active composition comprising a biologically or therapeutically or prophylactically effective amount of a trehalose-6 phosphate phosphatase inhibitor selected by a test method according to any of claims 1 to 7 or a pharmaceutically acceptable salt, ester or pro-drug thereof.

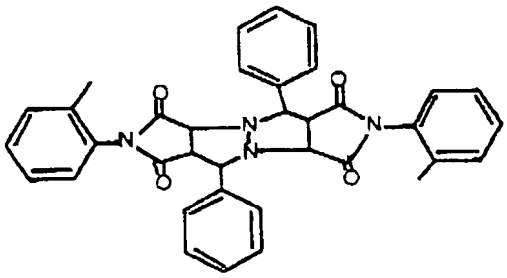
18. A biologically, prophylactically or therapeutically active composition according to claim 17, wherein the trehalose-6 phosphate phosphatase inhibitor is selected from the group consisting of substances with the structural formula :



or the structural formula



or the structural formula:



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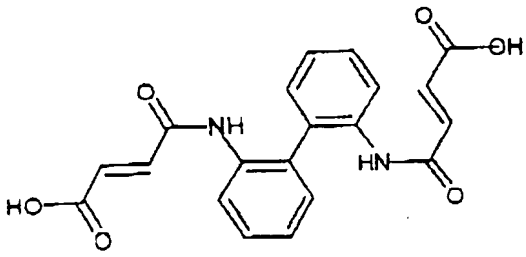

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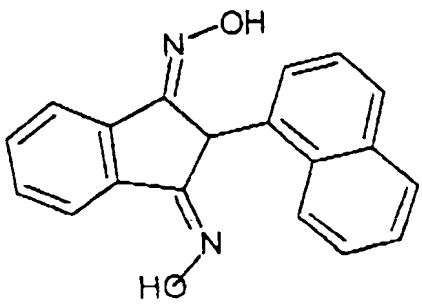
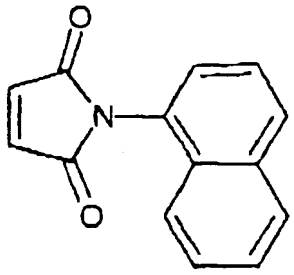
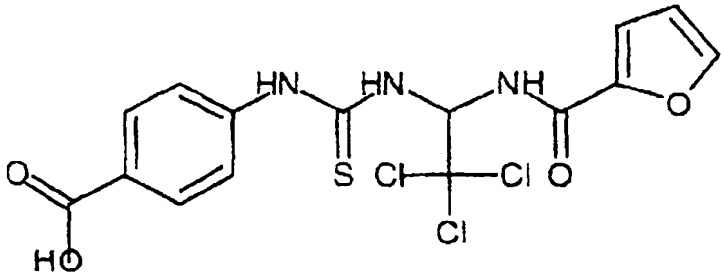


or the structural formula:



or the structural formula:



or pharmaceutically acceptable salts, esters or pro-drugs thereof.

19. A biologically, prophylactically or therapeutically active composition according to claim 17 or claim 18, further comprising an antiparasitic agent and/or a stress raising factor, i.e. a compound that induces or enhances the stress response of cells.

20. A biologically, prophylactically or therapeutically active composition according to claim 19, wherein the antiparasitic agent and/or stress raising factor is an azole.

21. A biologically, prophylactically or therapeutically active composition according to claim 19, wherein the antiparasitic agent and/or stress raising factor is one of amphotericin B, flucytosine, ketoconazole, miconazole, fluconazole and itraconazole.

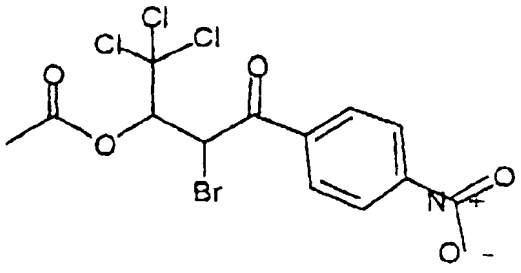
22. A biologically, prophylactically or therapeutically active composition according to any of claims 18 to 21, being a biocide acting on fungi, insects, nematodes, bacteria, protozoa, worms, mites or other organisms accumulating increased quantities of trehalose under stress conditions.

23. A method of increasing trehalose-6-phosphate content in a plant, yeast, fungal, bacterial, protozoan, nematode or other worm, mite or insect cell, comprising the step of reducing the activity of trehalose-6 phosphate phosphatase in the said cell by using a

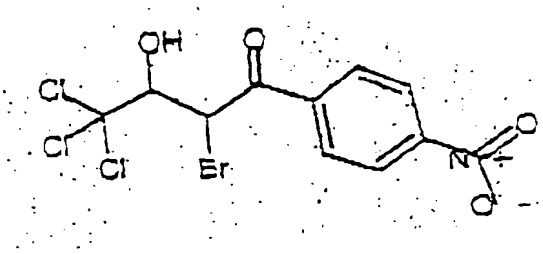
trehalose-6 phosphate phosphatase inhibitor.

24. A method of increasing trehalose-6-phosphate content according to claim 23, wherein the trehalose-6 phosphate phosphatase inhibitor is selected by a test method according to any of claims 1 to 7.

25. A method of increasing trehalose-6-phosphate content according to claim 23 or claim 24, wherein the trehalose-6 phosphate phosphatase inhibitor is selected from the group consisting of substances with the structural formula:



or the structural formula



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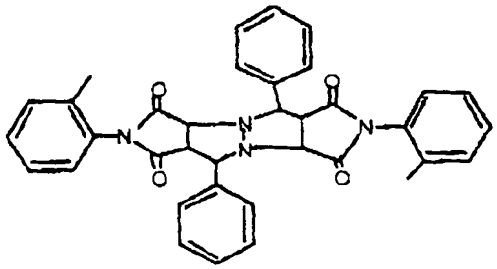
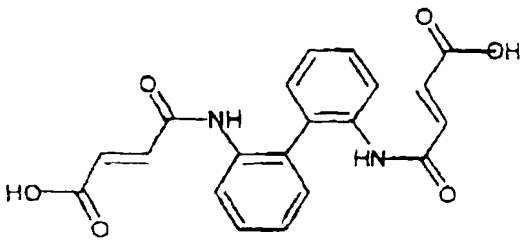


or the structural formula:



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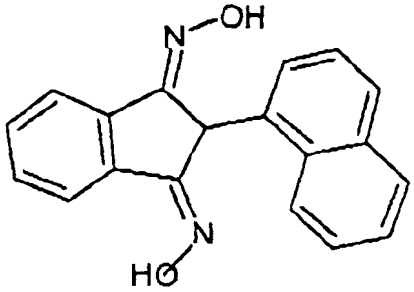
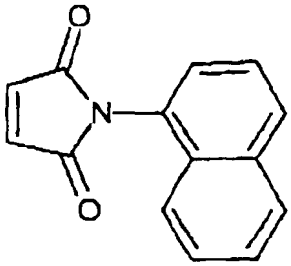
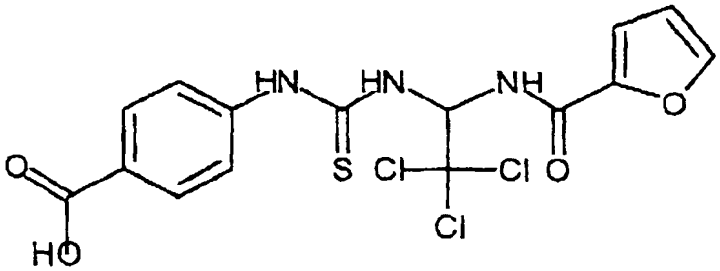


or the structural formula:



or the structural formula:



or pharmaceutically acceptable salts, esters or pro-drugs thereof.

26. A method of increasing trehalose-6 phosphate content in a yeast, fungal, bacterial, protozoal, nematodal, worm, mite or insect cell, comprising the step of reducing or inhibiting the activity of trehalose-6 phosphate phosphatase in the said cell by a single or double knockout deletion mutation of trehalose-6 phosphate phosphatase.

27. A method of reducing or impairing the pathogenecity of a mammalian parasite by

promoting hyperaccumulation of trehalose-6 phosphate in the cells of the said parasite.

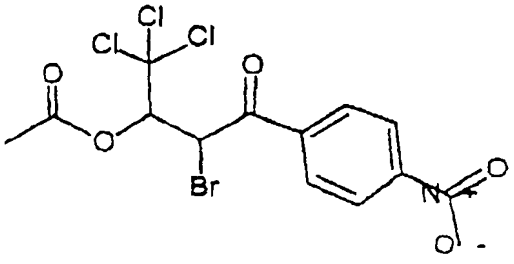
28. A method for preventing or treating a parasitic infection of a human or animal, comprising administering a therapeutically or prophylactically effective amount of a trehalose-6 phosphate phosphatase inhibitor selected by a test method according to any of claims 1 to 7 or a pharmaceutically acceptable salt, ester or pro-drug thereof.

29. A method for preventing or treating a parasitic infection of a plant, comprising administering a therapeutically or prophylactically effective amount of a trehalose-6 phosphate phosphatase inhibitor selected by a test method according to any of claims 1 to 7 or a pharmaceutically acceptable salt, ester or pro-drug thereof.

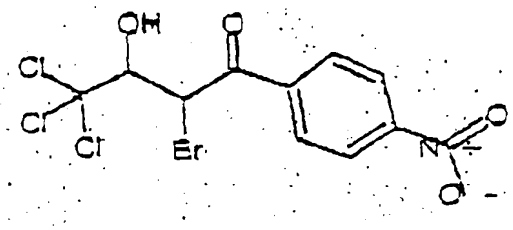
30. A method for preventing or treating a parasitic infection according to claim 28 or claim 29, wherein administration is effected topically.

31. A method for preventing or treating a parasitic infection according to claim 28 or claim 29, wherein administration is effected systemically.

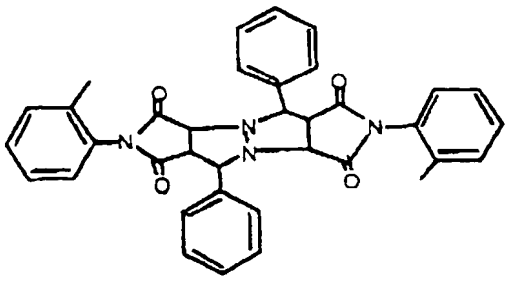
32. A method for preventing or treating a parasitic infection according to any of claims 28 to 31, wherein the trehalose-6 phosphate phosphatase inhibitor is selected from the group consisting of substances with the structural formula:



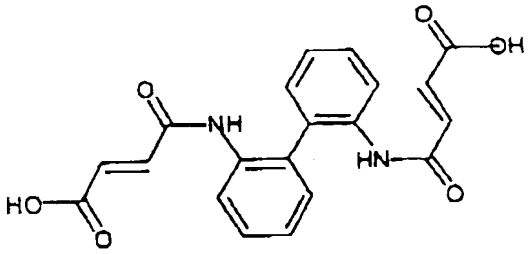
or the structural formula



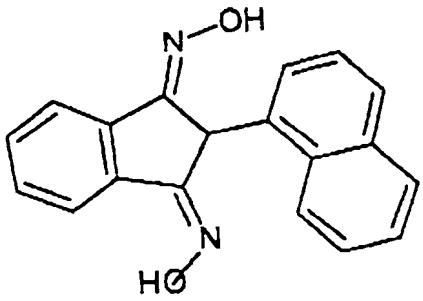
or the structural formula:



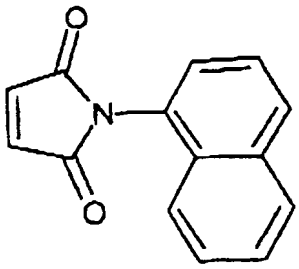
or the structural formula:



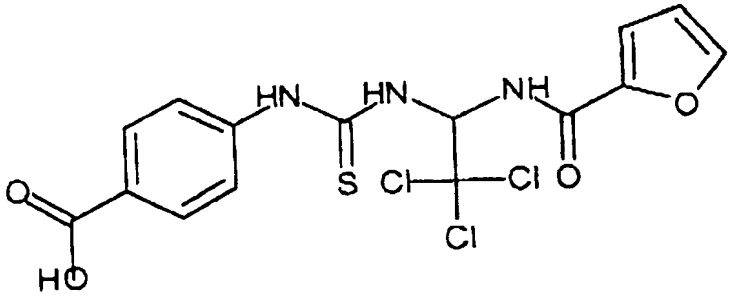
or the structural formula:



or the structural formula:



or the structural formula:



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA.

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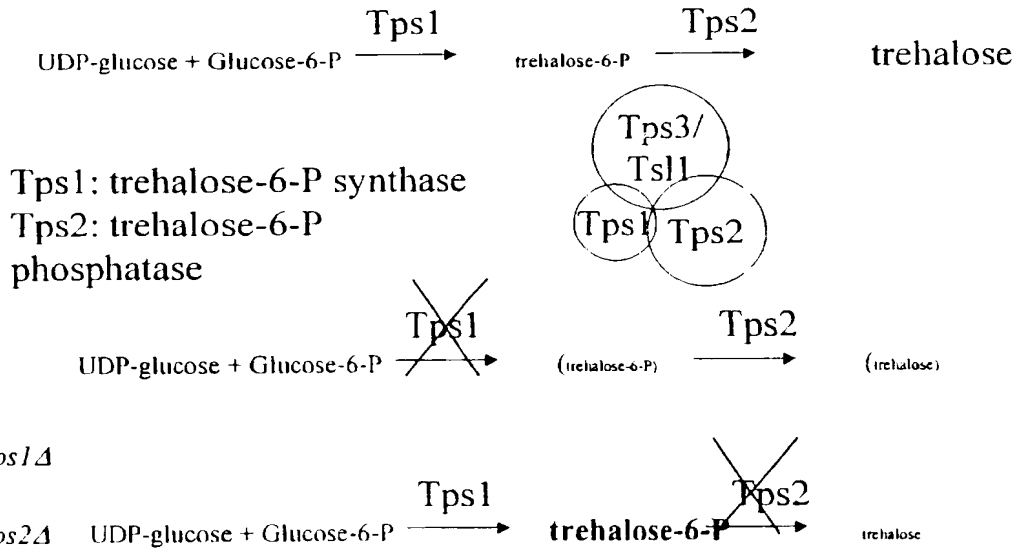
Published:
— *with international search report*

[Continued on next page]

(54) **Title:** NOVEL TARGET FOR ANTIPARASITIC AGENTS AND INHIBITORS THEREOF



(57) **Abstract:** The use of an enzyme found in fungi, bacteria, insects, nematodes, worms, mites, protozoa etc. as a target in a screening assay is described by means of which agents capable of inhibiting the function of that enzyme may be identified. The screening assay may include complete cell or purified-enzyme assays. In particular, the present invention relates to a screening assay for inhibitors or suppressors of sugar alcohol phosphatases or sugar phosphatases, and more in particular inhibitors or suppressors of trehalose-6-phosphate phosphatase, as well as preparations, in particular, pharmaceutical preparations, which include inhibitors or suppressors obtained from the screening assay. Inhibitors are described as well as applications in biocides and antifungal pharmaceuticals.

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(88) Date of publication of the international search report:
29 November 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 00/08410

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/42 C12Q1/18 A01N61/00 A61K35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 29894 A (EPPS DENNIS E ;UPJOHN CO (US); MARSCHKE CHARLES K (US)) 17 June 1999 (1999-06-17) the whole document ---	1-13
A	WO 96 17066 A (BYK GULDEN LOMBERG CHEM FAB ;MELCHERS KLAUS (DE)) 6 June 1996 (1996-06-06) abstract ---	1-13
A	US 5 759 795 A (JUBIN RONALD G) 2 June 1998 (1998-06-02) the whole document ---	1-13

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 January 2001	08. 02 2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hoekstra, S

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
A	HOHMANN S ET AL: "EVIDENCE FOR TREHALOSE-6-PHOSPHATE-DEPENDENT AND -INDEPENDENT MECHANISMS IN THE CONTROL OF SUGAR INFLUX INTO YEAST GLYCOLYSIS" MOLECULAR MICROBIOLOGY,GB,OXFORD, vol. 20, no. 5, page 981-991 XP000615219 the whole document	1-13
A	THEVELEIN J M ET AL: "TREHALOSE SYNTHASE: GUARD TO THE GATE OF GLYCOLYSIS IN YEAST ?" TIBS TRENDS IN BIOCHEMICAL SCIENCES,EN,ELSEVIER PUBLICATION, CAMBRIDGE, vol. 20, no. 1, page 3-10 XP002020937 ISSN: 0968-0004 the whole document	1-13
A	GOUNALAKI, N AND THIREAOS, G.: "Yap1p, a yeast transcriptional activator that mediates multidrug resistance, regulates the metabolic stress response" THE EMBO JOURNAL, vol. 13, no. 17, 1994, pages 4036-4041, XP002129348 the whole document	1-13
A	WO 97 31107 A (COLES JOHN G ;YOUNG DAVID S F (CA); BROCKHAUSEN INKA (CA)) 28 August 1997 (1997-08-28) page 70, line 25 - line 28	1-13
A	DATABASE PROMT 'Online! AN 96:60687, 30 January 1996 (1996-01-30) "DIVERSet 96 a breakthrough chemical library for lead generation now available for drug discovery community." XP002151748 abstract & "DIVERSet 96 a breakthrough chemical library for lead generation now available for drug discovery community." BUSINESS WIRE, 30 January 1996 (1996-01-30), page 01300250 Chicago the whole document	1-13

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP 00/08410

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 14-17 in part and 37-40 completely
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy (Claims 37-40).

2. [X] Claims Nos.: 14-17 in part
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-13 and 23 entirely, 14-17 and 26-36 in part (Compound 143067)

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 14-17 in part

Present claims 14-17 relate to a product defined by reference to a desirable characteristic or property, namely inhibiting sugar- or sugar alcohol-, phosphate phosphatase activity. The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently a search shall, conditional to the payment of any additional fees under Article 17(3)(a), be carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to any of the specified compounds of claim 18-15.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Subject 1/92: Claims 1-13

   Test method for assessing the activity of candidate substances as inhibitors of sugar-phosphate phosphatases.

2. Claims: Subject 2/92: Claims 14-17, 25-36 in part and 18 entirely

   compound 100764

3. Claims: Subject 3/92: Claims 14-17 and 26-36 in part and 19 entirely

   The compound of claim 19

4. Claims: Subject 4/92: Claims 14-17, 25-36 in part and 20 entirely

   Compound 135235

5. Claims: Subject 5/92: Claims 14-17 and 26-36 in part and 21 entirely

   Compound 133207

6. Claims: Subject 6/92: Claims 14-17 and 26-36 in part and 22 entirely

   Compound 113610

7. Claims: Subject 7/92: Claims 14-17 and 26-36 in part and 23 entirely

   Compound 143067

8. Claims: Subject 8/92: Claims 14-17 and 26-36 in part and 24 entirely

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Compound 113596

9. Claims: Subjects 9/92 - 92/92: Claims 14-17 and 25-36 in part

Each of the 84 separate compounds from the list of claim 25 which are not present in subjects 2-8 (compounds 100764 and 135235) is a further separate invention in the sense of Article 17(3)(a), last sentence.

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Inter...l Application No
PCT/EP 00/08410

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9929894 A	17-06-1999	AU 1703499 A	28-06-1999
		EP 1036192 A	20-09-2000
WO 9617066 A	06-06-1996	DE 4442970 A	05-06-1996
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		AU 4259096 A	19-06-1996
		EP 0797669 A	01-10-1997
		JP 10509875 T	29-09-1998
		US 5981184 A	09-11-1999
US 5759795 A	02-06-1998	NONE	
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